Unraveling the effects of rhythmic external cueing on mobility: synchronisation and use of alternative circuitry in the parkinsonian brain.

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To identify neurophysiological mechanisms (e.g. synchronisation / desynchronisation) and brain areas (i.e. localization) involved in the performance of cued movements in PD.

Ethical review	Approved WMO
Status	Pending
Health condition type	Neuromuscular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON29887

Source
ToetsingOnline

Brief title
Unraveling cueing in parkinson's disease

Condition

- Neuromuscular disorders

Synonym
Parkinson's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Internationaal Parkinson Fonds

Intervention

Keyword: parkinson cueing rhythm brain

Outcome measures

Primary outcome

Group and condition differences in 1) localization, latency and amplitude of evoked cortical potentials, 2) spectral power over different frequency bands, 3) cortico-cortical synchronization patterns (e.g. interregional coupling or correlation, synchronization likelihood, coherence), 4) blood oxygen level-dependent (BOLD) MRI signal changes.

Secondary outcome

Group differences in changes in performance on motor paradigm after rTMS (hand movement speed, timing of hand movement to cues and walking speed, cadence and stride length).

Study description

Background summary

See protocol.

Rationale:
External rhythmic cues have a positive effect on movement and specifically gait and gait-related activities in patients with Parkinson*s disease (PD, (www.rescueproject.org). Cueing can be defined as *applying temporal or spatial stimuli associated with the initiation or ongoing facilitation of motor activity (e.g. gait)*. However, the underlying mechanisms are largely unknown. The current project is designed to investigate the following research question: which neurophysiological mechanisms and brain areas are involved when patients with PD adapt to external rhythmic cueing conditions? In a first experimental series, magnetoencephalography (MEG) and combined electroencephalography/functional magnetic resonance imaging (EEG/fMRI) will be used to record brain activity during motor tasks in the recumbent position. In

a second experimental series repetitive transcranial magnetic stimulation (rTMS) will be used to alter the excitability of selected brain areas (e.g. supplementary motor area, SMA).
It is hypothesized that rhythmic external cues act 1) by resetting pathological oscillatory neural activity and/or 2) through bypassing of the defective basal ganglia circuitry via alternative neural pathways. Resetting of pathological oscillatory activity is thought to result from coupling processes between brain area*s induced by external rhythms through, for example, attentional processes. It is further hypothesized that following selective transient inhibition of the SMA using rTMS, cued motor activity will show degraded performance. It is anticipated that knowledge about these mechanisms will be useful in optimizing the effectiveness of rehabilitation therapy using rhythmic external cues

Study objective

To identify neurophysiological mechanisms (e.g. synchronisation / desynchronisation) and brain areas (i.e. localization) involved in the performance of cued movements in PD.

Study design

cross-sectional, observational study.
Intervention: in a first session (1 day), subjects perform an experimental motor paradigm (hand-squeezing movements) in a MEG and MRI apparatus. Brain activity will be recorded during, as well as before and after the cued motor paradigm. In addition, rTMS will be applied in a second session (on a second day) prior to a hand motor paradigm, as well as a number of walking tests.

Study burden and risks

Overall, the risks associated with participation are minimal and estimated to be acceptable bij the investigators, when compyling with the exclusioncriteria. The burden of time-investment and physical performance of the motor paradigm in the MEG and MRI as well as before and after rTMS are recognized and will be explained in detail to prospective participants. Subjects will receive a set of 8 questionnaires to be completed at home by regular mail. The number of site visits to the Outpatient department of the VU University Medical Center will be 2, one for each experimental series. The interval between the sessions will depend on completion of the first session for all participants.
The first visit will entail : 1) short motor examination (incl. motor section of the Unified Parkinson*s Disease Rating Scale [UPDRS]), 2) performance of a motor paradigm (cued hand-movements) in the MEG apparatus and 3) a motor paradigm (cued hand-movements) in the MRI apparatus. These measurements of brain activity are non-invasive, safe and applied on a routine basis in the VUmc. The physical and physiological discomfort is recognized, but estimated to be at an acceptable level, and subjects will receive adequate rest periods an

breaks between assessments and conditions.
The second visit will entail: Assessment of motor performance before and after a 15 minute rTMS session. Application of rTMS is non-invasive, safe and applied routinely in the VUmc.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients: 1) Modified Hoehn and Yahr stage ranging from 2 to 4; 2) a stable medication regime;
All: 3) age under 70 years; 4) sufficient orientation in time and place (Minimal Mental State Examination (MMSE) * 26) , 5) completion of an informed consent for participation, and 6) able to walk 10 meter independently.

Exclusion criteria

Patients: 1) Presence of severe dyskinesia (Modified Dyskinesia Scale score >1),
All: 2) any (other) neurological, cardiovascular or orthopaedic disorder or other co-morbidity that may influence mobility and would interfere with participation ,3) presence of medical implants such as pacemakers, 4) inability to communicate (written of verbally) in the Dutch language and 5) history fo epilepsy

Study design

Design

Study phase:	2
Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	10-01-2006
Enrollment:	45
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL13811.029.06